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The investigations indicate that the diastatic power of the saliva of pellagra patients is at least as great as that of normal people. In no case, whether the flow of saliva was scanty or very copious, was the diastatic power lacking.

While the amount of mucus precipitated from saliva by acetic acid was greater for the saliva of the pellagra patients than for the controls, the increase is apparently unrelated to the severity of the symptoms, either general or oral.

The study of the sulphocyanate content of the saliva disclosed that this is much less marked in the case of pellagra patients than it is in the saliva of normal people. Since it is generally admitted that the sulphocyanate arises from the metabolism of protein and the detoxicating action of the system, whereby poisonous cyanides are converted into the relatively innocuous sulphocyanate, the investigators believe that in the pellagra patients there is both a lessened protein intake and a detoxicating power feebler than normal.

The reaction of the saliva in pellagra is somewhat more alkaline than is that of normal saliva.

THE SCHICK TEST AND ACTIVE IMMUNIZATION AGAINST DIPHTHERIA.

One of the pioneers in the introduction of diphtheria antitoxin into this country, and in other measures for the administrative control of diphtheria, the New York City Health Department is taking steps to secure the adoption of two additional measures for the control of this disease, namely, the employment of the Schick test in order to discover susceptible individuals and the active immunization of such individuals by means of toxin-antitoxin mixtures.

In their WEEKLY BULLETIN of March 15, the New York authorities call attention to the fact that, although there has been a continuous reduction in the death rate from diphtheria, "the mortality from this disease is still much higher than it should be, when we consider the armamentarium at hand for preventive and curative work." In New York City, despite the excellent results of antitoxin treatment, diphtheria still causes over 1,000 deaths annually, approximately 20 per 100,000 population. Rates only a little less than this prevail in Rhode Island, Pennsylvania, Kentucky, North Carolina, Massachusetts, and Michigan.

As a result of extensive studies by means of the Schick test conducted under the direction of Dr. W. H. Park, mainly among the charges of various child-caring institutions, it has been found that susceptibility to diphtheria is present in about the following proportions:

Age:	Per cent susceptible.
Under 3 months	15
3 to 6 months	30
6 months to 1 year	60
1 to 2 years	70
2 to 3 years	60
3 to 5 years	40
5 to 10 years	30
10 to 20 years	20
Over 20 years	15

THE SCHICK REACTION.

"The Schick reaction is a convenient and reliable clinical test, by which the antitoxic immunity of an individual to diphtheria can be determined. A fresh solution of diphtheria toxin is prepared for this purpose of such strength that 0.1 cc. or 0.2 cc. represents 1/50 of the minimum lethal dose of toxin for a 250-gram guinea pig. This amount is injected with a good syringe, preferably a 1 cc. 'Record' and a fine steel or platinum-iridium needle, *intracutaneously* on the flexor surface of the forearm or arm. A good guide for the insertion of the needle into the proper layer of the skin is to be able to see the oval opening of the needle through the superficial layers of the epidermis. A properly made injection is recognized by a distinct wheal-like elevation, which shows the prominent openings of the hair follicles. The result of the test should be read at the end of 24, 48, 72, and 96 hours.

"The reaction that appears at the site of injection may be either positive, negative, pseudo, or combined positive and pseudo.

"The *positive* reaction represents the action of an irritant toxin upon tissue cells that are not protected by antitoxin. It indicates, therefore, an absence of immunity to diphtheria. A trace of redness appears slowly at the site of injection in from 12 to 24 hours, and usually a distinct reaction in the course of 24 to 48 hours. The reaction reaches its height on the third or fourth day, and gradually disappears, leaving a definitely circumscribed scaling area of brownish pigmentation, which persists for 3 to 6 weeks. At its height the positive reaction consists of a circumscribed area of redness and slight infiltration, which measures from 1 to 2 cm. in diameter. The degree of redness and infiltration varies to a great extent with the relative susceptibility of the individual. The positive reaction is seen in about 7 to 10 per cent of the new-born, 30 per cent during the first year of life, 35 decreasing to 15 per cent between 2 and 14 years, and 10 per cent of adults.

"In the *negative* reaction the skin at the site of injection remains normal. The negative reaction definitively indicates an immunity to diphtheria if the test-toxin is of full strength, has been freshly diluted, and the injection has been made into the proper layer of the skin. A negative reaction obtained in a child that has reached the age of 3 years indicates that it has an immunity which is probably permanent. Of 1,000 carefully observed individuals, not one developed clinical diphtheria, even though they were exposed to the disease, and some were carriers of virulent diphtheria bacilli.

"The *pseudo-reaction* represents a local anaphylactic response of the tissue cells to the protein substance of the autolyzed diphtheria bacilli, which is present in the toxic broth used for the test. Like other anaphylactic skin phenomena, the reaction is of an urticarial nature, appears early within 6 to 18 hours, reaches its height in 36 to 48 hours, and disappears on the third or fourth day, leaving a poorly defined small area of brownish pigmentation and generally no scaling. At its height the pseudo-reaction shows varying degrees of infiltration, and appears as a small central area of dusky redness with a second areola, which gradually shades off into the surrounding skin. The reaction may also have a rather uniform red appearance, and be two or three times the size of true reaction. A control test, made by injecting toxin heated to 75° C. for 5 minutes, gives a similar reaction which passes through the same clinical course. Individuals who give a pseudo-reaction only, have antitoxin and are immune to diphtheria. The false reaction is seen in relatively few of the older children, but in a much larger number of adults, in whom it is of importance to recognize and control it both by the injection of heated toxin and by observing the clinical course of the reaction.

"The *combined* reaction represents the positive and the pseudo-reaction in the same individual. The central area of redness is larger and better defined, the amount of infiltration is also more marked. The reaction is recognized by noting the evidence of a true reaction, a definitive area of scaling brownish pigmentation, after the pseudo-element has disappeared in the test. In addition, a similar though weaker reaction is obtained in a control test made with heated toxin. The control represents only the pseudo-reaction. The combined reaction indicates an absence of immunity to diphtheria.

"The Schick test is of practical value in determining the immunity to diphtheria of the public in general, but especially of the child population in schools, hospitals, institutions, and in homes during an outbreak of diphtheria. It will save a considerable amount of antitoxin and avoid unnecessary sensitization of more than 65 per cent of the exposed individuals. The test is also of distinct value in the active immunization of susceptible individuals against diphtheria with mixtures of toxin-antitoxin, and in the diagnosis of clinically doubtful cases of diphtheria."—Text of a circular of information issued by the department of health, city of New York.

As supplied by most manufacturers, the Schick test outfit consists of a tube of diphtheria toxin and a vial containing a measured amount of sterile salt solution. By mixing the contents of the capillary tube with the saline a solution is obtained which is ready to be injected into the skin.

The following is the text of directions given by a manufacturer for the use of the Schick test outfit:

"Break off one end of the capillary tube, push the broken end carefully through the neck of the rubber bulb until it punctures the diaphragm within and enters the cavity of the bulb; then break off the other end of the tube. Hold the bulb between thumb and middle finger, place the index finger over the opening in the larger end of the bulb and expel the toxin into the 10 cc. of saline. Rinse out the capillary tube by drawing up saline several times, then cork the bottle and shake the diluted toxin. Inject 0.1 cc. or 0.2 cc., representing 1/50 M. L. D. for the guinea pig, *intracutaneously* on the flexor surface of the forearm or arm. The contents of the bottle are sufficient for about 35 tests. On account of the fairly rapid deterioration, it is not advisable to use the diluted toxin after 12 to 24 hours. The outfit must be kept very cold to prevent deterioration.

"A uniform technique in the intracutaneous injection is essential in the Schick test. A good guide for the insertion of the needle into the proper layer of the epidermis is to be able to see the oval opening of the needle through the superficial layers of cells. A definite wheal-like elevation, with the distinct markings of the openings of the hair follicles, shows that the injection has been made properly and that the fluid is confined to a small area of the epidermis. Here it will exert its irritant action, if the individual tested is not immune to diphtheria.

"Syringes and needles: Preferably a 1 cc. 'Record' tuberculin syringe and a fine platinum-iridium or steel needle. An ordinary hypodermic syringe with a fine steel needle may be used in emergencies."

ACTIVE IMMUNIZATION.

After discovering susceptible individuals by means of the Schick test, the question at once arises as to how best to immunize these individuals. The protection afforded by injections of diphtheria antitoxin is of very short duration, three or four weeks being the usual period. Far more lasting is the protection afforded by active immunization. During the past three years Park and his coworkers have employed active immunization with toxin-antitoxin mixtures in the case of over 4,000 susceptibles (including 1,000 infants under 1 week old), without the subsequent occurrence of a single case of diphtheria. Park summarizes his observations as to the value of this active immunization as follows:

> The procedure is absolutely harmless. No reaction develops in infants, while in older children and adults a moderate swelling of the arm may appear and last for from one to three days.
>
> One injection gives immunity to 80 per cent of those previously susceptible; two injections give immunity to 90 per cent; and three injections to 97 per cent.
>
> The immunity conferred lasts for at least three years and probably much longer.
>
> No diphtheria has occurred in those so far immunized.

In order to facilitate active immunization by practicing physicians, several establishments making biological products put up small vials containing a mixture of diphtheria toxin-antitoxin. This mixture is used undiluted. The dose is 1 cc. injected subcutaneously in the arm at the insertion of the deltoid. The injection is repeated at weekly intervals until three injections have been given. For children under 1 year of age the dose is 0.5 cc. In the younger children the local and constitutional symptoms following the injections of toxin-antitoxin are much less marked than in older children and adults. The difference is due to a greater susceptibility of the older children to the diphtheria bacillus protein, which is present in the mixture of toxin-antitoxin.

Determining the Effect of Active Immunization.

The development of an active immunity is determined at the end of three months by means of the Schick test. It has been found that the development of antitoxin in many individuals is often a slow process requiring from 8 to 12 weeks before a sufficient amount is produced to inhibit the Schick reaction. The number of successfully immunized individuals who will show a negative Schick retest after three injections of toxin-antitoxin will be, in different groups, from 90 to 99 per cent.

Indications for Active Immunization with Toxin-Antitoxin.

The use of toxin-antitoxin for active immunization may be considered under two heads.

1. *As a general prophylactic measure.*—The most suitable age period for testing and immunizing is between 6 months and 2 years. At this time of life the percentage of positive Schick reactions is largest and the susceptibility to diphtheria as well as the mortality from the disease is greatest. Children of this age period can be reached in the homes, in infant asylums, in the milk stations, and day nurseries. The children of the next age period are included in the preschool groups. These children can be reached in the public

schools, in orphan asylums, and in the various other institutions. Among adults, those who come in contact with diphtheria and are constantly exposed and in danger should also be tested and immunized with toxin-antitoxin if found to give a positive Schick reaction. Included in this group are especially physicians, nurses, and hospital attendants in contagious disease hospitals.

2. *To control an outbreak of diphtheria.*—As the immunity arising from an injection of toxin-antitoxin does not develop until the lapse of from 2 to 12 weeks, active immunization can not be utilized to protect persons from exposure within that period. In institutions, however, where small outbreaks of diphtheria have occurred, or where diphtheria is more or less constantly present and clinical cases and bacillus carriers steadily appear, the use of antitoxin alone has often been insufficient to stamp out the disease, but the combined application of the Schick test and active immunization with toxin-antitoxin has given successful and encouraging results. Toxin-antitoxin immunization should not be used with antitoxin immunization in the same individual, as the surplus antitoxin tends to prevent the development of an active immunity.

BIOCHEMICAL STUDIES OF THE SALIVA IN PELLAGRA.

By M. X. Sullivan, Biochemist, and K. K. Jones, Food Analyst, Pellagra Hospital, United States Public Health Service, Spartanburg, S. C.

It is well established that in pellagra the alimentary tract is involved. Of the digestive tract, the oral cavity is of considerable importance in the diagnosis of pellagra, since the condition of the tongue is of much significance. The true pellagra tongue is vividly red and more or less swollen. Other parts of the oral cavity are likewise involved.

Since the oral cavity is of importance in the diagnosis of pellagra, a reconnoissance survey of the mixed saliva of individual pellagrins was started to determine wherein, if at all, the saliva, from a biochemical standpoint, differs from that of normal individuals. The study of the saliva included the rate of flow, the specific gravity, the total solids, the ash, the diastatic power, mucin, sulphocyanate, and abnormal constituents such as urea, uric acid, phenols, and indican.

The patients were inmates of the pellagra hospital of the United States Public Health Service at Spartanburg, S. C. Cases of pellagra reported by the medical staff as uncomplicated were taken for study. The work began April 12, 1917, and continued to June 19, and covered all practically uncomplicated cases of pellagra in the hospital during that period. During the time the saliva study was going on, only six of the patients, cases 294, 297, 303, 325, 327, and 338 were